

Claims

1. A process for the preparation of a stable hydrate mix of a compound, or a composition comprising the compound, the compound being capable of forming a plurality of hydration forms of differing stability and of dissolution to give a solution that, when frozen below the eutectic point, is a eutectic mixture, comprising:
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- a) providing a quantity of an aqueous mixture containing the compound or composition thereof in a suitable vessel in a freeze-drying apparatus;
- b) reducing the temperature in the apparatus to bring about freezing and eutectic solidification;
- 10 c) reducing the pressure in the apparatus to below the saturation vapour pressure (SVP) of water over ice at the temperature of the ice;
- d) maintaining the apparatus at a pressure below the SVP and, optionally, increasing the temperature in the apparatus to facilitate sublimation, until all of the ice has been sublimed;
- e) maintaining the apparatus at the pressure and temperature conditions according to step d) until
- 15 the desired water content has been obtained; and
- f) either:
- increasing the pressure in the apparatus to from about 60% to about 100% of atmospheric pressure (about 60.8 kPa to about 101.3 kPa) and subsequently adjusting the temperature in the apparatus to from about 5°C to about 30°C;
- 20 or
- adjusting the temperature in the apparatus to from about 5°C to about 30°C and subsequently increasing the pressure in the apparatus to from about 60% to about 100% of atmospheric pressure (about 60.8 kPa to about 101.3 kPa).
- 25 2. A process according to claim 1 wherein the temperature of step b) is from about -10°C to about -50°C.
3. A process according to claim 1 wherein the temperature of step b) is from about -20°C to about -40°C.
- 30 4. A process according to claim 1 wherein the temperature of step b) is about -30°C.
5. A process according to claim 1 wherein the pressure in step c) is from about 1Pa to about 250Pa.
- 35 6. A process according to claim 1 wherein the pressure in step c) is from about 2Pa to about 125Pa.

7. A process according to claim 1 wherein the pressure in step c) is from about 4Pa to about 75Pa.
8. A process according to claim 1 wherein the temperature in step d) is from about -50°C to about 50°C.
- 5 9. A process according to claim 1 wherein the temperature in step d) is from about -25°C to 0°C.
- 10 10. A process according to claim 1 wherein the temperature in step d) is about -15°C.
11. A process according to claim 1 wherein the drying process is monitored by applying a standard pressure rise test in the freeze drying apparatus.
12. A process according to claim 11 wherein the drying process is monitored at intervals of about one hour.
- 15 13. A process according to claim 1 wherein the duration of step (e) is from 0 to 100 hours.
14. A process according to claim 1 wherein the duration of step (e) is from 0 to 50 hours.
- 20 15. A process according to claim 1 wherein the duration of step (e) is from 6 to 30 hours.
16. A process according to claim 1 wherein the compound or composition comprises the disodium salt of fosfluconazole.
- 25 17. A process according to claim 12 wherein, the final water content of the stable hydrate mix is from about 11% to about 20% w/w.
18. A process according to claim 12 wherein, the final water content of the stable hydrate mix is from about 14% to about 17% w/w.
- 30 19. A process according to claim 12 wherein, the final water content of the stable hydrate mix is about 15% w/w.
20. The disodium salt of fosfluconazole in the form of its trihydrate, its hexahydrate, or as a mixture of tri- and hexahydrates.
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